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Introduction

Gastro-oesophageal reflux disease is a potentially serious condition that can greatly reduce patients' quality of life and carries a risk of oesophagitis and complications.[1] It is a common condition and a considerable burden on healthcare resources. Most patients are managed in general practice, and effective management of the disease remains a challenge. Guidelines produced in Europe,[2,3] the United States,[4] and Canada[5] do not give consistent recommendations.

Methods

An international multidisciplinary workshop was held in Genval, Belgium, in 1999 to evaluate the literature on gastro-oesophageal reflux disease, including numerous reviews,[6-8] in the light of clinical experience.[9] Participants voted on their level of support and the strength of the evidence for a series of statements relevant to the management of the disease. In this article we summarise the conclusions of the Genval workshop and present an overview of the latest thinking on the management of gastro-oesophageal reflux disease relevant to general practice. We also reviewed relevant articles published since the workshop, which we identified by a search of the electronic databases Medline and Embase from 1997 to March 2000, using the search term gastro-oesophageal reflux in combination with various key words for drug therapy, surgery, cost effectiveness, and quality of life.

Definition of gastro-oesophageal reflux

Gastro-oesophageal reflux disease should be diagnosed in all patients who are at risk of physical complications from gastro-oesophageal reflux or whose wellbeing is appreciably impaired because of symptoms related to reflux.[7,9] Most patients do not have endoscopically visible lesions, and symptoms are the main consideration. Heartburn is the predominant symptom of gastro-oesophageal reflux disease, and patients' quality of life is impaired in proportion to the frequency and severity of heartburn,[9] irrespective of the presence or severity of oesophagitis. The impact of symptoms on quality of life is similar to that of symptoms of other disorders such as ischaemic heart disease.[10] A recent large study using the SF-36 questionnaire showed the negative effect of gastro-oesophageal reflux disease on quality of life, notably on measures of pain, mental health, and social function.[11] Symptoms are mainly due to the oesophageal mucosa being exposed to acid and pepsin, and some patients may have a more sensitive mucosa than others.

Summary points

- Careful analysis of symptoms and history is key to diagnosis of gastro-oesophageal reflux disease
- Diagnosis based on symptoms can be aided by a trial of treatment
- Clear endoscopic abnormalities are found in less than half of patients
- Treatment should start with the most effective therapy—a proton pump inhibitor
- Most patients will require long term management, for which the guiding principle is to reduce to the least costly treatment that is effective in controlling symptoms
- Antireflux surgery may be as effective as long term proton pump inhibitors but is less predictable

How reliable is diagnosis based on symptoms and what can be done to aid it?

Although gastro-oesophageal reflux disease is still commonly misdiagnosed as dyspepsia, the two problems are distinct and require different management. The Rome II working group defined dyspepsia as pain or discomfort centred in the upper abdomen.[12] This definition excludes heartburn, the primary symptom of gastro-oesophageal reflux disease. Careful analysis of the patient's symptoms and history is pivotal in the diagnosis and subsequent management of gastro-oesophageal reflux disease. Recognition of alarm symptoms (see box on endoscopy) is important in determining the need for referral.

Diagnosis of gastro-oesophageal reflux disease is usually based on the occurrence of heartburn on two or more days a week, although less frequent symptoms do not preclude disease.[9 13] A standard against which to compare heartburn is still lacking for patients without oesophagitis.[7 9] Nevertheless, when heartburn is carefully defined, it is unlikely to be due to anything other than gastro-oesophageal reflux disease; indirect evidence and clinical experience show that three quarters of patients in whom heartburn is the main or sole symptom have gastro-oesophageal reflux disease.[9] When inquiring about patients' symptoms it is important to give a definition of heartburn. For example, the description of heartburn as "a burning feeling rising from the stomach or lower chest up towards the neck" has been found to identify more patients with gastro-oesophageal reflux disease than use of the word itself.[9 14] Diagnosis may be improved by the use of a structured diagnostic questionnaire or by a trial of treatment, as described below.

When should patients be referred for endoscopy?

Less than half of patients with gastro-oesophageal reflux disease have diagnostic endoscopic abnormalities, and endoscopy therefore has a limited role in diagnosis. Endoscopy is, however, useful in some patients for clarification of diagnosis, assessing severity of disease, recognition of the complications of oesophagitis, and for defining best treatment strategies (box). No consensus exists on its precise role or on when it is best performed.[15 16] The use of endoscopy will depend on local cost, accessibility, and timing relative to treatment. Most patients should be managed empirically, at least initially.

The questions of whether to look for Barrett's oesophagus, and what to do when it is found, are controversial and difficult.[17] Affected patients have an increased risk of oesophageal adenocarcinoma, but views on surveillance vary widely. If patients are known to have Barrett's oesophagus, surveillance endoscopy is probably advisable. General practitioners should be guided by the opinion of a gastroenterologist.[17] More information is available in the current practice guidelines.[18]

The results of endoscopy need to be reported in a standardised, defined language that is explicit and unambiguous. The report should explain the implications of the findings for patient care and, in particular, be sceptical about the diagnostic validity of minimal endoscopic changes (erythema, oedema, friability). We recommend the Los Angeles classification for endoscopic assessment and reporting of oesophagitis.[9 19 20] In addition, the possible effects of treatment should be borne in mind when interpreting the results of endoscopy. Repeat endoscopy is rarely justified in patients without severe oesophagitis. Monitoring of oesophageal pH should be reserved for patients in whom the diagnosis is in doubt after endoscopy and a trial of acid suppressing drugs.

Indications for early endoscopy

Alarm symptoms (including dysphagia, weight loss, bleeding, abdominal mass)
Diagnostic problems such as atypical symptoms
Symptoms refractory to initial treatment
Preoperative assessment
Provision of reassurance when verbal reassurance is inadequate

Endoscopy may also be appropriate:
For patients who have had frequent, troublesome symptoms for a long time
To tailor drug treatment
To detect and manage Barrett's oesophagus

Hierarchy of efficacy for drug treatments (most effective first)[9]

High dose proton pump inhibitors
Standard dose proton pump inhibitors
Half dose proton pump inhibitors
Standard dose H_2-receptor antagonists
Antacids

Effectiveness of different drugs

The hierarchy of efficacy of therapies in gastro-oesophageal reflux disease (box) has been well established in randomised clinical trials,[9] although data on half dose proton pump inhibitors relate to its use in long term intermittent therapy rather than initial therapy.[9 21 22] The relative effectiveness is unaffected by the presence of endoscopic oesophagitis or whether treatment is short or long term. Long term safety and tolerability have been extensively documented for H_2 receptor antagonists and proton pump inhibitors.[23]

Cisapride has similar effectiveness to standard dose H_2 receptor antagonists but is inferior to standard dose omeprazole.[24] When combined with an H_2 receptor antagonist, it is more effective than either treatment alone,[25] but the risks of cardiac side effects with cisapride now exclude it from routine use in reflux disease.

Strategies for initial treatment

Explanation of the symptoms and reassurance of the patient (for example, addressing concerns about cancer and heart disease) are an important part of initial treatment. General practitioners should also consider lifestyle measures and self treatment, such as antacids, which the patient may already be using. Some lifestyle measures provide limited benefit in gastro-oesophageal reflux disease. Avoidance of specific foods and drinks that exacerbate symptoms may help, although it does not usually result in healing of the oesophagitis.[9] Although stopping smoking and losing weight are of benefit to the patient's general health, they have little or no effect on gastro-oesophageal reflux disease.

There are two approaches to the initial medical treatment of gastro-oesophageal reflux disease. Treatment can either start with the most effective regimen and subsequently be stepped down or start with the minimum intervention and be stepped up. There are arguments in favour of both approaches (box). The

Advantages and disadvantages of step-down and step-up treatment

Regimen	Advantages	Disadvantages
Step-down treatment (high initial therapy)	Rapid symptom relief Efficient for doctor Avoids overinvestigation and associated costs	Potential overtreatment Higher initial drug cost
Step-up therapy (minimum initial therapy)	Avoids overtreatment Lower initial drug cost	Patient may continue with symptoms unnecessarily Takes too long Inefficient for doctor May lead to overinvestigation Uncertain end point (partial symptom relief)

higher initial drug cost when beginning with the most effective regimen is likely to be offset by rapid symptom control, which is a substantial benefit to the patient and reduces the need for repeated consultation. We recommend starting with the most effective treatment,[9] which is currently standard dose of a proton pump inhibitor. This treatment is also the preferred choice for empirical therapy.

Although empirical therapy will test a provisional diagnosis, a formal therapeutic trial[9] in which a proton pump inhibitor is given in greater than standard dose for 1-2 weeks can also be used. This test has a sensitivity and specificity for gastro-oesophageal reflux disease comparable to that of monitoring oesophageal pH.

After the initial treatment, it is worth trying a period without treatment because some patients will not need further medical intervention, at least for several months.[26] Patients in whom symptoms immediately recur require longer term management.

Eradication of *Helicobacter pylori* does not heal oesophagitis or prevent relapse in patients with gastro-oesophageal reflux.[9] However, there is likely to be a complex interaction between acid secretion, eradication of *H pylori,* and exposure of the oesophagus to acid in certain patients.

Strategies for long term management

Most patients with gastro-oesophageal reflux disease require long term management.[27,28] The guiding principle for long term management is to step down to the treatment that is least costly but still effective in controlling symptoms, following the hierarchy described above.[9] The rationale for this approach is minimisation of cost, although relative drug costs will vary across practice settings, and decreasing efficacy does not always mean decreasing cost. Finding the right level of management may take time in some patients.

Patients returning with a relapse after a trial without treatment should be restarted on the initial successful therapy and then have treatment stepped down as appropriate. For patients who require only intermittent short courses of antisecretory therapy, it may be more effective to give a proton pump inhibitor at full dose than to titrate treatment up from either half dose of proton pump inhibitor or standard dose of a H_2 receptor antagonist.[26]

A further component in optimising use of resources is the minimal use of endoscopy. The success of a step down in treatment can largely be determined by symptoms alone. If a patient's symptoms are successfully controlled, the general practitioner can be confident that oesophagitis will have healed in most cases,[9] and endoscopy is unnecessary. The comfort and convenience of patients are further reasons to minimise use of endoscopy.

The only patients in whom treatment should not be stepped down are those with severe oesophagitis (Los Angeles grades C and D). Treatment other than standard dose proton pump inhibitors is unlikely to prevent relapse of oesophagitis or strictures in these patients.[9] Endoscopy is not always necessary as it is safe to assume that oesophagitis is healing in patients whose symptoms are controlled. Patients with inadequate symptom control should be referred for endoscopy.

Antireflux surgery is an attractive option for some patients as it can eliminate the need for life long drug treatment. It should not be reserved for patients in whom drugs have failed. Open antireflux surgery and long term proton pump inhibitors have been shown to be equally effective over a follow up of five years.[29] Patients' preferences for medical or surgical treatment should be taken into account. Data on the safety of long term use of proton pump inhibitors suggest that this is safer option than antireflux surgery, which has a small but probably inevitable mortality of around 0.2% and appreciable morbidity. The laparoscopic approach, introduced 10 years ago, has superseded open antireflux surgery, but surgeons have to develop and maintain special skills to get consistently good results.[30]

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1 Lagergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999;340:825-31.
2 Kroes RM, Numans ME, Jones RH, deWit NJ, Verheij TJM. GERD in primary care. Comparison and development of European guidelines on gastroesophageal reflux disease. *Eur J Gen Pract* 1999;5:88-97.
3 French-Belgian Consensus Conference on Adult Gastro-oesophageal Reflux Disease. Diagnosis and treatment report of a meeting held in Paris, France on 21-22 January 1999. The jury of the consensus conference. *Eur J Gastroenterol Hepatol* 2000;12:129-37.
4 DeVault KR, Castell DO, Practice Parameters Committee of American College of Gastroenterology. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* 1999;94:1434-42.
5 Thomson ABR, Chiba N, Armstrong D, Tougas G, Hunt RH. The second Canadian gastroesophageal reflux disease consensus: moving forward to new concepts. *Can J Gastroenterol* 1998;12:551-6.
6 Kahrilas PJ. Gastroesophageal reflux disease. *JAMA* 1996;276:983-8.
7 Dent J. Gastro-oesophageal reflux disease. *Digestion* 1998;59:433-45.
8 Galmiche JP, Letessier E, Scarpignato C. Treatment of gastro-oesophageal reflux disease in adults. *BMJ* 1998;316;1720-3.

9 Dent J, Brun J, Fendrick AM, Fennerty MB, Janssens J, Kahrilas PJ, et al. An evidence-based appraisal of reflux disease management—the Genval workshop report. *Gut* 1999;44(suppl 2):S1-16.
10 Dimenas E. Methodological aspects of evaluation of quality of life in upper gastrointestinal disease. *Scand J Gastroenterol* 1993:28(suppl 199):18-21.
11 Revicki DA, Wood M, Maton PN, Sorensen S. The impact of gastroesophageal reflux disease on health-related quality of life. *Am J Med* 1998;104:252-8.
12 Talley NJ, Stanghellini V, Heading RC, Kock KL, Malagelada JR, Tytgat GNJ. Functional gastroduodenal disorders. *Gut* 1999;45(suppl 2):II37-42.
13 Glise H. Quality of life and cost of therapy in reflux disease. *Scand J Gastroenterol* (suppl) 1995;210:38-42.
14 Carlsson R, Dent J, Bolling-Sternevald E, Johnsson F, Junghard O, Lauritsen K, et al. The usefulness of a structured questionnaire in the assessment of symptomatic gastroesophageal reflux disease. *Scand J Gastroenterol* 1998;33:1023-9.
15 Blustein PK, Beck PL, Meddings JB, Van Rosendaal GMA, Bailey JR, Lalor E, et al. The utility of endoscopy in the management of patients with gastroesophageal reflux symptoms. *Am J Gastroenterol* 1998;93: 2508-12.
16 Gillen D, McColl KE. Does concern about missing malignancy justify endoscopy in uncomplicated dyspepsia in patients aged less than 55? *Am J Gastroenterol* 1999;94:2329-30.
17 Spechler SJ, Goyal RJ. The columnar-lined oesophagus, intestinal metaplasia, and Norman Barrett. *Gastroenterology* 1996;110:614-21.
18 Sampliner RE, Practice Parameters Committee of American College of Gastroenterology. Practice guidelines on the diagnosis, surveillance, and the therapy of Barrett's esophagus. *Am J Gastroenterol* 1998;93: 1028-32.
19 Armstrong D, Bennett JR, Blum AL, Dent J, De Dombal FT, Galmiche JP, et al. The endoscopic assessment of oesophagitis: a progress report on observer agreement. *Gastroenterology* 1996;111:85-92.
20 Lundell LR, Dent J, Bennett J, Blum AL, Armstrong D, Galmiche JP, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut* 1999;45: 172-80.
21 Bate CM, Green JRB, Axon ATR, Tildesley G, Murray FE, Owen SM, et al. Omeprazole is more effective than cimetidine in the prevention of recurrence of GERD-associated heartburn and the occurrence of underlying oesophagitis. *Aliment Pharmacol Ther* 1998;12:41-7.
22 Bardhan KD, Cherian P, Vaishnavi RB, Jones RB, Thompson M, Morris P, et al. Erosive esophagitis: outcome of repeated long-term maintenance treatment with low dose omeprazole 10 mg or placebo. *Gut* 1998;43: 458-64.
23 Klinkenberg-Knol EC, Nelis F, Dent J, Snel P, Mitchell B, Prichard P, et al. Long-term omeprazole treatment in resistant gastroesophageal reflux disease: efficacy, safety and influence on gastric mucosa. *Gastroenterology* 2000;118;661-9.
24 Hatlebakk JG, Hyggen A, Madsen PH, Walle PO, Schulz T, Mowinckel P, et al. Heartburn treatment in primary care: randomised, double blind study for eight weeks. *BMJ* 1999;319:550-3.
25 Vigneri S, Termini R, Leandro G, Badalamenti S, Pantalena M, Savarino V, et al. A comparison of five maintenance therapies for reflux esophagitis. *N Engl J Med* 1995;333:1106-10.
26 Bardhan KD, Müller-Lissner S, Bigard MA, Bianchi Porro G, Ponce J, Hosie J, et al. Symptomatic gastro-oesophageal reflux disease: double blind controlled study of intermittent treatment with omeprazole or ranitidine. *BMJ* 1999;318:502-7.
27 Gambitta P, Indriolo A, Colombo P, Grosso C, Pirone Z, Rossi A, et al. Management of patients with gastroesophageal reflux disease: a long-term follow-up study. *Current Ther Res* 1998;59:275-87.
28 McDougall NI, Johnston BT, Collins JSA, McFarland RJ, Love AHG. Three to 4.5-year prospective study of prognostic indicators in gastroesophageal reflux disease. *Scand J Gastroenterol* 1998;33:1016-22.
29 Lundell L. Miettinen P, Myrvold HE, Pedersen SA, Thor K, Andersson A, et al. A randomised comparison between omeprazole and open anti-reflux surgery in the management of chronic gastro-oesophageal reflux disease: report on 5 year follow up [abstract]. *Gut* 1999;45 (suppl 5):A40.
30 Lundell L. Miettinen P, Myrvold HE, Pedersin Sa, Thor K, Lamm M, et al. Long-term management of gastro-oesophageal reflux disease with omeprazole or open anti-reflux surgery: results of a prospective, randomised clinical trial. *Eur J Gastroenterol Hepatol* 2000;12:879-87.

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A memorable patient

Escape by water

Our trekking party in north eastern Nepal had ascended to the magical Thyangboche Monastery at 3800m. We continued our descent and return journey through the village of Namche Bazaar (3400m) in high spirits, after completion of our mission. Suddenly our thoughts were interrupted when an anxious Sherpa raced up behind me. He told me that a doctor was needed and rushed me breathlessly back up the hill. I wrongly assumed that all of our party were ahead of me and wondered if I was being taken to sort out a medical problem in the village.

I was shown into one of the lodge rooms at Namche that we had left earlier. One member of our party, an extremely fit 25 year old, was lying on the bed indisposed, with our trek leader bent over him, massaging his chest. He was pale and sweaty with distended neck veins and a rapid heartbeat. The palpitations had started suddenly an hour earlier. He was feeling faint, nauseous, and generally frightened by the unexpected situation.

His radial pulse was almost impalpable, but, taking his carotid pulse, I assumed this to be a supraventricular tachycardia. I felt almost useless without medical equipment or monitors in this high, isolated village. We tried some Valsalva manoeuvres, followed by carotid sinus massage, each with no effect. Searching the depths of my mind for inspiration, I suddenly remembered the diving reflex. I asked for a bowl of cold water and, without warning, plunged the patient's head into it. Much commotion followed trying to remove the patient's soaking wet sweater and drying his hair with a towel. It was difficult to ascertain the precise moment he returned to sinus rhythm, but it had certainly happened. The palpitations had disappeared and he was feeling much better. I too was feeling much relieved as my next plan would probably have involved an ex-Russian army helicopter.

Meanwhile, the rest of the party had trekked on down the scenic Dudh Kosi valley with much speculation about the nature of the emergency and no means of establishing what was happening higher up. A helicopter flew up and down the valley. The day passed by and our party arrived at the new lodge, tired and breathless. Everyone was keen to hear the exciting story and relieved there were no serious problems.

It transpired that there had been a death at Everest Base Camp, presumably from acute mountain sickness. The helicopter sent to collect the body had crashed in the valley killing the accompanying trek leader and the pilot. This was the helicopter the rest of the group had spotted that day, now lying shattered on the rocks. Faced with this terrible reality we suddenly understood the potential dangers of our adventure and for once in my life I was extremely glad that we had not had to rely on emergency repatriation as our last treatment option.

Jenny Tye *registrar in anaesthesia, Birmingham*

We welcome articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake,* or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.